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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,918	12/28/2001	Rajiv Shah	047711-0293	2208

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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
09/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/035,918	SHAH ET AL.	
	Examiner	Art Unit	
	Yong D. Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,12-15,18-24,44 and 45* is/are pending in the application.

4a) Of the above claim(s) *25-43 and 48-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-8, 10-24 and 44-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Notification of Non-Compliant Appeal Brief (37 CFR 41.37)	Application No. 10/035,918	Applicant(s) SHAH ET AL.	
	Examiner Yong Pak	Art Unit 1652	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

The Appeal Brief filed on *02 April 2007* is defective for failure to comply with one or more provisions of 37 CFR 41.37.

To avoid dismissal of the appeal, applicant must file anamended brief or other appropriate correction (see MPEP 1205.03) within **ONE MONTH or THIRTY DAYS** from the mailing date of this Notification, whichever is longer. **EXTENSIONS OF THIS TIME PERIOD MAY BE GRANTED UNDER 37 CFR 1.136.**

1. ☒ The brief does not contain the items required under 37 CFR 41.37(c), or the items are not under the proper heading or in the proper order.

2. ☐ The brief does not contain a statement of the status of all claims, (e.g., rejected, allowed, withdrawn, objected to, canceled), or does not identify the appealed claims (37 CFR 41.37(c)(1)(iii)).

3. ☐ At least one amendment has been filed subsequent to the final rejection, and the brief does not contain a statement of the status of each such amendment (37 CFR 41.37(c)(1)(iv)).

4. ☒ (a) The brief does not contain a concise explanation of the subject matter defined in each of the independent claims involved in the appeal, referring to the specification by page and line number and to the drawings, if any, by reference characters; and/or (b) the brief fails to: (1) identify, for each independent claim involved in the appeal and for each dependent claim argued separately, every means plus function and step plus function under 35 U.S.C. 112, sixth paragraph, and/or (2) set forth the structure, material, or acts described in the specification as corresponding to each claimed function with reference to the specification by page and line number, and to the drawings, if any, by reference characters (37 CFR 41.37(c)(1)(v)).

5. ☐ The brief does not contain a concise statement of each ground of rejection presented for review (37 CFR 41.37(c)(1)(vi))

6. ☐ The brief does not present an argument under a separate heading for each ground of rejection on appeal (37 CFR 41.37(c)(1)(vii)).

7. ☐ The brief does not contain a correct copy of the appealed claims as an appendix thereto (37 CFR 41.37(c)(1)(viii)).

8. ☒ The brief does not contain copies of the evidence submitted under 37 CFR 1.130, 1.131, or 1.132 or of any other evidence entered by the examiner **and relied upon by appellant in the appeal**, along with a statement setting forth where in the record that evidence was entered by the examiner, as an appendix thereto (37 CFR 41.37(c)(1)(ix)).

9. ☒ The brief does not contain copies of the decisions rendered by a court or the Board in the proceeding identified in the Related Appeals and Interferences section of the brief as an appendix thereto (37 CFR 41.37(c)(1)(x)).

10. ☒ Other (including any explanation in support of the above items):

The claimed invention is not mapped to the independent claim 1, which shall refer to the specification by page and line number and to the drawings, if any. The brief is missing headings Evidence Appendix and Related Proceedings Appendix, if there are none an indication of "None" or "Not Applicable" is required.

Bridget C. Monroe

BRIDGET C. MONROE
PATENT APPEAL CENTER SPECIALIST

DETAILED ACTION

In view of the Appeal Brief filed on June 6, 2007, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing at the end of this Action.

Claims 1, 3-8, 10-46 and 48-54 are pending. Claims 25-43 and 48-54 are withdrawn. Claims 1, 3-8, 10-24 and 44-46 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 and claims 3-8, 10-24 and 44-47 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the phrase "determining whether the colonies contain active glucose oxidase comprises: detecting a concentration of active glucose oxidase". It is not clear to the Examiner how the concentration of only active glucose oxidase is detected. Further, it is not clear how a concentration of glucose oxidase is detected from the colonies unless the glucose oxidase is first isolated. Therefore, the claim lacks essential steps: isolation step and detecting concentration of only active glucose oxidase. Examiner requests clarification of the claimed method.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that one of ordinary skill in the art would understand the cited phrase because various methods may be used to detect active glucose oxidase. Examiner respectfully disagrees. Although techniques in detecting enzymes are known, it is not clear how the concentration of only active glucose oxidase or glucose oxidase are detected.

Hence the rejection is maintained.

Claims 11 and 46 and 12-18 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 11 and 46 recite the term "testing the sensor". The metes and bounds of the term in the context of the claims are not clear. It is not clear to the Examiner what is encompassed by "testing the sensor" and what "testing the sensor" accomplishes in the methods. Examiner requests clarification of the above term.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-5, 12-15, 18-24 and 44-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Valdes et al., Cherry et al. and Hatzinikolaou et al.

Claims 1, 3-5, 12-15, 18-24 and 44-45 are drawn to a method of formulating or producing mutant glucose oxidases by obtaining a library of glucose oxidase genes, creating a library of mutated glucose oxidase genes by the methods recited in claims 20-24, introducing each mutated glucose oxidase genes into separate expression vectors, inserting said vectors into host organisms recited in claim 19, growing colonies of the host organism, determining whether the colonies contain active glucose oxidase by the methods recited in claims 3-5, 12-15, 18-24 and 44-45 and determining whether the colonies are resistant to peroxide and then measuring the concentration of the glucose oxidase.

Valdes et al. (cited previously on form PTO-892) discloses that glucose oxidase in glucose sensors are degraded by peroxide and this "decay can lead to the eventual failure of the senor" (abstract and page 367). Valdes et al. teaches that to ensure longer sensor functionality, instead of replacing the sensor with fresh enzyme, as has been practiced in the art, techniques to "prevent the degradation of the enzyme" is advantageous (page 375). With this teaching at hand, one having ordinary skill in the art would conclude that glucose oxidase may be prevented by using chemical agents, as suggested by Valdes et al. or to use glucose oxidase mutants that are resistant to peroxide since methods of generating mutants having resistance to chemicals are

known in the art, as discussed below. Valdes et al. also teaches a method of determining activity of glucose oxidase (page 370.

The difference between the reference of Valdes et al. and the instant invention is that the reference of Valdes et al. does not teach a method of producing mutant glucose oxidase that is resistant to degradation from peroxide. However, there are many methods widely available in the art of creating mutant genes by random mutations and screening for mutants displaying desired functional properties, such as having resistance to a chemical, such as a peroxide.

Cherry et al. (form PTO-892) discloses a method of making mutants of an enzyme which is also degraded in the presence of hydrogen peroxide by using directed evolution techniques, both DNA shuffling and error prone PCR (abstract). Cherry et al. discloses that after multiple rounds of directed evolution an enzyme, mutants of said enzyme that are resistant to deactivation in the presence of high concentration of hydrogen peroxide, conditions that mimic of hydrogen peroxide wherein the enzyme is normally deactivated, were obtained (pages 380-382). Cherry et al. discloses that colonies having enzymatic activity were selected to determine for its resistance against hydrogen peroxide (page 382).

Hatzinikolaou et al. (form PTO-892) discloses a library of glucose oxidase genes known in the art, such as *A. Niger* (page 371). Hatzinikolaou et al. also discloses a method of isolating and purifying glucose oxidase as recited in claims 14-18 and methods of measuring glucose oxidase activity and concentration of glucose oxidase (pages 372-373).

Therefore, combining the teachings of Valdes et al., Cherry et al. and Hatzinikolaou et al., it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to apply the method of Cherry et al. to formulate or produce mutant glucose oxidases having resistance to peroxide by generating a library of mutated genes using the glucose oxidase gene of Hatzinikolaou et al., transforming *E. coli* with vectors comprising each of the mutated genes, growing colonies of said cells and determining whether the colonies have active glucose oxidase followed by determining whether the colonies or the glucose oxidase comprised in the colony are resistant to peroxide and then test for the functionality of the glucose oxidase in a glucose sensor. One of ordinary skill in the art would have been motivated to produce mutant peroxide resistant glucose oxidases in order to use them in glucose sensors, thereby prolonging their use, since Valdes et al. teaches that glucose oxidases in glucose sensors are degraded by peroxide, leading to failure of the sensor. One of ordinary skill in the art would have had a reasonable expectation of success since Hatzinikolaou et al. teaches glucose oxidase genes and Cherry et al. teaches a comparable method of generating a library of mutant having resistance to hydrogen peroxide. Therefore, using the known technique of Cherry et al. to generate mutants of an enzyme having resistance against hydrogen peroxide would have been obvious to one of ordinary skill in the art.

Therefore, the above references render claims 1, 3-5, 12-15, 18-24 and 44-45 *prima facie* obvious.

Claims 16-17 rejected under 35 U.S.C. 103(a) as being unpatentable over Valdes et al., Cherry et al. and Hatzinikolaou et al. as applied to claims, 1, 3-5, 12-15, 18-24 and 44-45 above, and further in view of MIXONIX.

Claims 16-17 are drawn to a method of formulating or producing mutant glucose oxidases, wherein colonies comprising said mutant glucose oxidase is disrupted via sonication.

Valdes et al., Cherry et al. and Hatzinikolaou et al. in combination teaches a method of formulating or producing mutant glucose oxidases, as discussed above.

The difference between the reference of Valdes et al., Cherry et al. and Hatzinikolaou et al. and the instant invention is that said references do not teach a method of disrupting cells via sonication.

However, disrupting cells via sonication, through the use of a sonicator, during protein purification is well known and routinely practiced in the art, see MISONIX (form PTO-892).

Therefore, combining the teachings of Valdes et al., Cherry et al. and Hatzinikolaou et al. and MISONIX, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to disrupt cells comprising mutant glucose oxidase via sonication. One of ordinary skill in the art would have been motivated to do so in order to disrupt cells comprising the mutant glucose oxidase. One of ordinary skill in the art would have had a reasonable expectation of success since disruption of cells using sonication is well known and practiced routinely in the art.

Therefore, the above references render claims 16-17 *prima facie* obvious.

Claims 6-8, 10-11 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Valdes et al., Stemmer and Hatzinikolaou et al. as applied to claims 1, 3-5, 12-15, 18-24 and 44-45 above, and further in view of Wagner.

Claims 6-8, 10-11 and 46 are drawn to a method of formulating or producing mutant glucose oxidases by obtaining a library of glucose oxidase genes, creating a library of mutated glucose oxidase genes, introducing each mutated glucose oxidase genes into separate expression vectors, inserting said vectors into host organisms, growing colonies of the host organism, determining whether the colonies contain active glucose oxidase by testing glucose oxidase in sensors and using fluorescence of a leuco-cryalsta-violet, and determining whether the colonies are resistant to peroxide.

Valdes et al., Cherry et al. and Hatzinikolaou et al. in combination teaches a method of formulating or producing mutant glucose oxidases, as discussed above.

The difference between the reference of Valdes et al., Cherry et al. and Hatzinikolaou et al. and the instant invention is that said references do not teach a method of determining whether the colonies contain active glucose oxidase by testing glucose oxidase in sensors and using fluorescence.

Wagner (EP 0 251 475 A1 - form PTO-892) discloses a method of determining glucose oxidase activity via a sensor by measuring fluorescence emission from a dye, wherein oxidation of glucose by active glucose oxidase reduces the fluorescence emission (pages 2-3). In the method of Wagner, the glucose oxidase is conjugated to a dye and immobilized in the sensor (page 3). Wagner also teaches that any fluorescent

dye sensitive to quenching of its fluorescence emission by oxygen can be used (page 5).

Aldrich Catalog (cited previously on form PTO-892) discloses a leuco-cryalsta-violet dye (page 1005).

Therefore, combining the teachings of Valdes et al., Cherry et al. and Hatzinikolaou et al., Wagner and Aldrich Catalog, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use the method of Wagner to ascertain activity of the glucose oxidase, wherein glucose oxidase is isolated and purified by the method taught by Hatzinikolaou et al. One of ordinary skill in the art would have been motivated to do so in order to determine whether the colonies comprising mutated glucose oxidases have active glucose oxidase. One of ordinary skill in the art would have had a reasonable expectation of success since Wagner teaches how to determine activity of glucose oxidase by measuring fluorescence emission from a dye, wherein oxidation of glucose by active glucose oxidase reduces the fluorescence emission.

Therefore, the above references render claims 6-8, 10-11 and 46 *prima facie* obvious.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

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